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RESEARCH ARTICLE

Survey for CMV, HSV-2 Infections and their Association with Congenital Anomalies, Baghdad

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Abstract

A characteristic of herpes family is lifetime latency after primary infection and reactivation of the latent virus can reoccur in infected individuals at any time. To reduce the incidence of congenital anomalies, abortion and neonatal herpes cases, identification of at risk mother is the aim of the current study. Our results showed that seropositivity of CMV and HSV-2 were 12.39% and 8.26% infected women of all tested samples, respectively. It is remarkable that viral infections caused congenital anomie and preterm delivery, because the percentages of these obstetric complications were 31.39% and 44.66% of all cases studied, respectively. Both CMV and HSV-2 are associated significantly more than 70% with abortion cases. Furthermore, 60% of pregnant women reported during first gestation trimester and begin to decline significantly in the late gestation for each virus, whereas approximately 50% of the viral infections and their complication were identified in women after losing a pregnancy. Although the two attributions of viral infections were low prevalence, the abortion and congenital anomalies were highly associated with these infectious agents. We recommended that all antenatal cases should be screened for these agents. In addition to DNA detection was conducted to allow assessment of the serological diagnosis.

Introduction

Cytomegalovirus (CMV) and Herpes simplex virus (HSV) are Herpesviridae family, and are among the most ubiquitous viruses in the adult population. A characteristic of this family is lifetime latency after primary infection and reactivation of the latent virus can reoccur in infected individuals at any time (Ziyaeyan et al., 2007).It is found universally throughout all the geographical locations and in the areas of low socioeconomic conditions. A majority of these infections are asymptomatic as others and they are difficult to diagnose clinically (Sen et al., 2012). Bad obstetric history (BOH) implies previous unfavorable fetal outcome in terms of two or more consecutive spontaneous abortions, early neonatal deaths, stillbirths, intrauterine fetal deaths, intrauterine growth retardations and congenital anomalies (Haider et al., 2011). Maternal infections play a critical role in pregnancy wastage and their occurrence in patients with BOH is a significant factor (Mookerjee et al., 1995). The presence of virus-specific Immunoglobulin M (IgM) may not be indicative of primary infection, since it is also produced during reactivation and re infection (Nielsen et al., 1988).

CMV is the most common cause of congenital malformation resulting from viral intrauterine infection in developing countries (Gaytant et al., 2002). The damage seems to be more severe in infections occurring during the first half of the pregnancy, while infections in the second half would result in reduced morbidity (Walters, 1992). Cytomegalovirus infection during pregnancy is more complex than other infections, due to virus reactivation during the child bearing age and be transmitted to the fetus in spite of maternal immunity (Mukundan et al., 1977). On the other hand, HSV infection of the newborn can be acquired in utero,intrapartum and postnatally (Anzivino et al., 2009). The mother is the usual source of transmission of HSV to the fetus or newborn. Primary HSV infection during the first half of pregnancy is associated with increased frequency of spontaneous abortion, stillbirth, and congenital malformation (Plotskin, 1999). Additional risk factors for neonatal HSV infection include the use of a foetal-scalp electrode and the age of the mother less than 21 years (Baker, 2007). Moreover, neonatal herpes is much more frequent (50%) in babies from mothers with a primary HSV infection respect to babies from mothers with recurrent HSV infection (<3%) (Ciavattini et al., 2007). Currently, the congenital anomalies and abortion are increased significantly in our population, and many studies identified these viruses, but as our knowledge there is no previous study containment of large sample size. To reduce the incidence of congenital anomalies, abortion and neonatal herpes cases, identification of at risk mother is the aim of the current study.

2. Materials and Methods

2.1. Study Population

A total of 2100 blood sample was collected from pregnant and non-pregnant women with bad obstetric histories, during period Nov. 2010 to Dec. 2012 from Baghdad hospitals. These women selected randomly with different ages from 17-46 years (25.5±7.831). Of these, 1646 women were tested for both CMV and HSV-2 infection, whereas 428 women were tested for CMV and 26 women for HSV-2 infection alone. A detailed case investigation was filled up for each one of them regarding their socioeconomic status, clinical signs and maternal history: gestation age, no. of previous pregnancies, preterm delivery, abortions and congenital children with their status.

2.2. Specific IgM Estimation

All Samples were stored at -20c till tested. The tests were done using IgM-ELISA Bio-kits reagents manufactured by Barcelona-Spain to detect anti-IgM specific for CMV and HSV-2, in accordance with the manufacture's instructions.

2.3. Statistical Analysis

The data and graphs were carried out using spss program version 20 IBM. The proportion and their frequencies were checked by applying the chi - square test. The P-values < 0.05 considered statistically significant.

3. Results

3.1 Cases

Our results showed that seropositivity for CMV and HSV-2 were 257 and 138 infected women of all tested samples, respectively. Of these infected women, 25 cases were harbor for both viruses. Prevalence of percentage for CMV and HSV-2 specific IgM were 12.39% and 8.26% of all samples tested, respectively. It is remarkable that viral infections caused congenital anomie and preterm delivery, because the percentages of these obstetric complications were 31.39% and 44.66% of all cases studied, respectively. (Table 1)

According to age groups, the highest infection observed in 20-30 age years of each virus. The significant difference in the age group was shown for both CMV and HSV-2 infections (P<0.01).

3.2. Obstetric complications

Figure 1 demonstrates that infected women with CMV and HSV-2 associated significantly more than 70% with abortion cases (P<0.000001). Meanwhile, approximately equal percentages of preterm delivery cases which caused by CMV and HSV-2 within the study population.

In the current study, we reported that CMV and HSV-2 infections significant correlation with infected women that had congenital anomalies (P<0.01). Seropositivity specific IgM for CMV and HSV-2 in the infected women with repeated pregnancy were compromised of 73.54% and 81.88%, respectively.

More than 60% of pregnant women reported during first gestation trimester and begin to decline significantly in the late gestation for each virus (Fig. 2).

Figure 3 shows that approximately 50% of the viral infections and their complication were identified in women after losing a pregnancy. Significant correlation of gestation trimester with viral infections and these two complications

was reported. Moreover, the significance accompanying of these viral infections with congenital anomie was showed (P<0.01).

Table 1: Distribution of infected women according to age groups that associated with infection type and obstetric complications

Age group/ year	No. of CMV +ve	No. of HSV-2 +ve	Abortion*	Congenital* anomie	Preterm* delivery
>20	39	23	43	15	4
20-30	163	88	177	73	35
31-47	55	27	59	25	7
Total	257	138	279	113	46

A steric refers to the no. of positive cases for either CMV or HSV-2 or both.

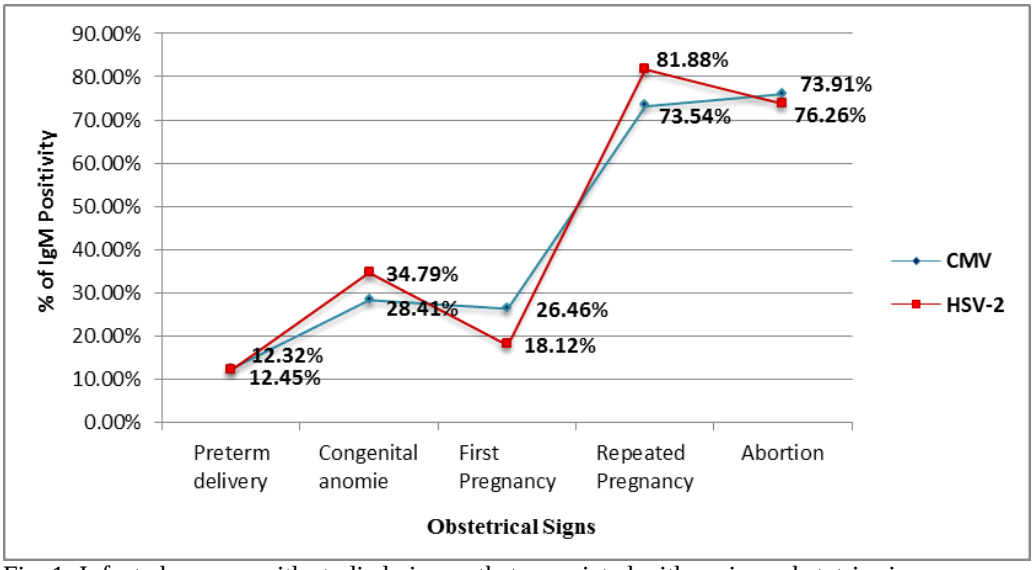

Fig. 1: Infected women with studied viruses that associated with various obstetric signs.

Here, some infected women had both studied viruses, there is highly significant between HSV-2 and congenital anomalies (P<0.000001).

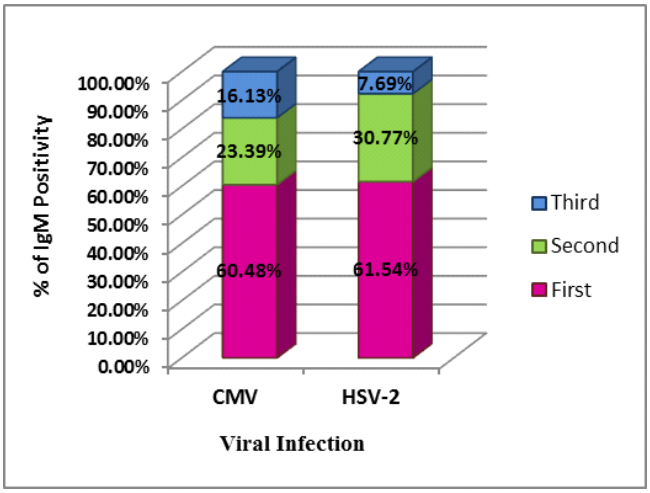

Fig. 2: Percentages of seropositivity for CMV and HSV-2 infections during gestation trimester

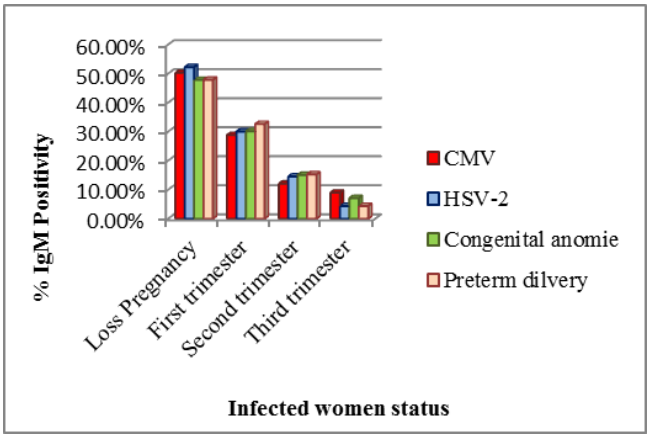

Fig. 3: Observation of infected women with congenital anomalies during and loss gestation trimester.

Here, the infected women during gestation trimester had congenital anomalies in previous pregnancy, all these viral infections and their complications showed statistically significant (P<0.000001).

4. Discussion

Here, 12.39% were had CMV IgM antibodies, while 8.26% were HSV-2. Other investigators reported the seropositive rate of CMV and HSV-2 IgM in women with Bad Obstetric Histories were 8.4%,34.7%, 29.5% and 33.5%, 16.8%, respectively (Turbadkar et al., 2003; Sen et al., 2012; Chopra et al., 2004; Haider et al., 2011). In Iraq, although our finding is lower than the result reported by Iraqi authors (46.6%, 66% of IgM CMV and 24.25 of IgM HSV-2) (Brooks et al., 2001; Al-Marzoqi et al., 2012; All-jumaili et al.,2013), it's similar that seropositive of CMV and HSV-2 are reported (15.7% and 17.3%, respectively) (Khalf et al., 2012; Al-Marzoqi et al., 2012), these differences may be studied due to sample size. In South America, available data are mainly for women, in whom HSV-2 prevalence ranges from 20% to 40%. Prevalence in the general population of Asian countries shows lower values, from 10% to 30% (Paz-Bailey et al., 2007; Weiss, 2004).

The presence of CMV-specific IgM may not be indicative of primary infection, since it is also produced during reactivation and reinfection (Nielsen et al., 1988). Though more women who are in the childbearing ages are already seropositive, reinfection with a new strain of CMV can cause infections even in the presence of detectable IgG levels (Boppana et al., 2001). HSV-2 prevalence has also been found to vary by individual-level characteristics, including gender, age, sexual activity level, marital status, socioeconomic status, education, and race/ethnicity (Xu et al., 2006). However, these characteristics are insufficient to explain differences within and between countries, regions, and population subgroups, suggesting the need to identify ecologic factors which may help to explain the differences (Smith and Robinson, 2002). Up to 15% of intrauterine CMV infections result in symptomatic congenital disease at birth, and 10 to 15% of those born with asymptomatic congenital CMV will develop significant clinical sequelae in infancy (Dahle et al., 2000; Fowler et al., 1997). In utero transmission of CMV can occur during primary maternal infection, reactivation, or reinfection of seropositive mothers. Most concern centers on primary maternal infection, due to the potential for significant fetal damage when the infection is acquired and transmitted during the first trimester (Gaytant et al., 2002; Kumar and Prokay, 1983).

Our study reported the highest infection that over 63% was between 20-30 years of age that similar to author (Al-Marzoqi et al., 2012). The greatest incidence of HSV infections occurs in women of reproductive age, the risk of maternal transmission of the virus to the fetus or neonate has become a major health concern (Kriebs, 2008;Cusini and Ghislanzoni, 2001). Age and sex are important risk factors associated with the acquisition of genital HSV-2 infection. In fact, the prevalence of HSV infection is very low in childhood and early adolescence but it rises with age, reaching the maximum around 40 years (Desselberger, 1998). Meanwhile, risk factors for CMV infection have been correlated with the socioeconomic status within a community (Fowler et al., 1993; 2003).

In this study, we gave a hint that pregnant women who had the IgM specific for CMV and HSV-2 are 30.77% and 7.69%, respectively at late trimester of pregnancy which are more likely to transmit the virus to their unborn child than women who are infected early in gestation (Haider et al., 2011). The risk of neonatal infection varies from 30% to 50% of HSV infections that onset in late pregnancy (last trimester), whereas early pregnancy infection carries a risk of about 1% (CDC, 2006). When primary HSV infection occurs during late pregnancy, there is not adequate time to develop antibodies needed to suppress viral replication before labor (Enright and Prober, 2002).

Furthermore, approximately 30% of each viral infection reported during first trimester of gestation that increases the risk of virus intrauterine transmission with advancing gestation. The first trimester of pregnancy is an

important period often fraught with complications like bleeding and pain, leading to severe apprehension in the mother (Florence et al., 1999). Moreover, some maternal infections, especially during the early gestation, can result in fetal loss or malformations because the ability of the fetus to resist infectious organisms is limited and the fetal immune system is unable to prevent the dissemination of infectious organisms to various tissues (Levett, 2005). The danger of intrauterine HSV transmission is highest during the first 20 weeks of gestation because it can lead to abortion, stillbirth and congenital anomalies (Sauerbrei and Wutzler, 2007).

The highest infection was reported in women who had repeated bad pregnancy with spontaneous abortion may due to primary or recurrent infection. Primary or recurrent herpes simplex virus (HSV) infection in pregnancy and its serious consequences for the fetus and neonate have attracted much interest. Specifically, primary HSV infection during the second or third trimester can be related to pre-term labor, fetal abnormalities and pregnancy loss, whereas recurrent HSV infection constitutes a much lower risk for the embryo, fetus and neonate (Kapranos and kotronias, 2009). In contrast, the association of HSV with first trimester pregnancy loss, despite the initial epidemiological observations has not been fully elucidated and remains controversial (Bujko et al., 1988). It is recognized that primary CMV infections occurring at an early gestational age are more likely to cause fetal damage than recurrent infections (Sarawathy et al., 2011). In cases of spontaneous abortion that HSV is a causative agent, there is a risk for later SAs in spite of the fact that HSV infection is not primary and this may occur even in the absence of clinical signs and symptoms (Bujko et al., 1988).

On the other hand, the infection with CMV and HSV-2 women at first pregnancy were 26.5% and 18.2%, respectively. Thus, consequences of primary HSV-2 infections on pregnancy outcome are thought to be more severe than of secondary infections (Maitra and Gupta, 2007), but some studies showed the relation between intrauterine latent HSV infection and spontaneous abortion (Robb et al., 1986). As a consequence of placental infection, CMV impairs cytotrophoblast differentiation and invasiveness; this could explain early abortion occurring in women with primary infection (Walters, 1992).

Conclusion

Although the two attributions of viral infections were low prevalence, the abortion and congenital anomalies were highly associated with infectious agents. The present study demonstrates that infectious agents linked with abortion and congenital anomalies in women with BOH. We recommended that all antenatal cases should be screened for these agents. In addition to DNA detection was conducted to allow assessment of the serological diagnosis.

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